employed, the only important considerations are to determine whether or not local or distant spread has occurred. Otherwise, with a patient in fairly good condition and satisfactory preoperative preparation, the Whipple operation is the procedure of choice if one wishes to make an attempt to cure his patient. It is a prolonged operation, quite shocking, but the ends to be achieved are worth the risk. It is performed in two stages. The first stage consists of double ligation of the common duct with heavy linen and its incision between these ligatures. The ligature on the distal end is left long for identification at the second stage. The small bowel is divided about 12 to 15 inches distal to the ligament of Treitz, an end-to-side enterostomy is performed, and the fundus of the gall-bladder is anastomosed to the distal end of the jejunum. This is all of the first stage. The second stage is performed two or three weeks later, following satisfactory recovery from the first operation. The distal end of the severed common duct is identified by its long ligature. Posterior gastroenterostomy is performed. The gastroduodenal artery is identified and ligated. The entire duodenum and a large wedge-shaped portion of the head of the pancreas are excised en bloc. The ducts of Santorini and Wirsung are ligated with heavy silk or linen, and the pancreatic remnant is ligated with interrupted sutures of silk. One drain is placed in the pancreatic bed so formed. While this operation is indeed radical and its immediate mortality high, it offers the only present opportunity for complete radical cure of malignant lesions in this region.

In a recent personal communication, Doctor Whipple stated that his present tendency is to perform the entire operation in one stage in individuals who are in good condition and seem able to tolerate it. The only feasible alternative procedure is an anastomosis between the gall-bladder and the intestinal tract, preferably the duodenum. This is to be performed when the growth has extended beyond limits permitting of its radical removal, or when the patient's condition will not permit consideration of the Whipple operation. It offers, at best, only temporary palliation, records showing that the average life expectancy after these palliative procedures is about seven and a half months.

SUMMARY

In the surgical management of lesions of the common duct, a thorough understanding of normal and abnormal liver physiology is essential.

Recent advances in our knowledge of liver function are applied to common-duct obstruction.

The surgical treatment of operative strictures and the management of common-duct stones are outlined.

Missed stone and its treatment are discussed.

The principles used in the successful treatment of carcinoma of the body elsewhere are equally applicable to carcinoma involving the common duct and its neighboring structures.

The Whipple operation presents a practical application of these principles.

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SYPHILIS: FIVE-DAY TREATMENT*

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THE five-day treatment of syphilis, as introduced by Hyman, Chargin, and Leifer,[1] represents an attempt to eradicate early syphilis by means of a massive dose of an arsenical spirocheticide administered intravenously by the continuous drip method. In 1931 Hirschfeld, Hyman, and Wagner[2] showed that large amounts of a toxic substance may be given intravenously without untoward reactions, provided this substance is introduced into the blood stream with sufficient slowness. They concluded that many of the toxic reactions which follow intravenous injections are the result of speed shock. Applying this principle to the treatment of early syphilis, Hyman, Chargin, and Leifer have attempted to reach Ehrlich's original goal, namely, the total sterilization of the patient from spirochetes by one massive dose of arsphenamin.

STUDIES AT MOUNT SINAI HOSPITAL

A symposium on this subject held at Mount Sinai Hospital, New York City, on April 12, 1940, created considerable interest in this work, among both medical men and the lay public. The importance of this investigation is indicated by Moore,[3] who, in discussing the papers presented on that occasion, stated: "This investigation may represent the most important advance in the treatment of syphilis since the original discovery of arsphenamin by Ehrlich in 1909." This method of treatment is still in the experimental stage and is being investigated by the group of workers at Mount Sinai Hospital. At this institution an organization has been set up for the proper execution of the technique and for a thorough follow-up of the patients from both the clinical and the laboratory standpoint. We agree with these workers that the administration of this treatment should be confined to that institution until its merits and dangers have been completely evaluated.

The purpose of this paper is to present a critical review of the published reports and to comment on certain aspects of the problems involved.

REVIEW OF PUBLISHED REPORTS

As a result of the symposium at Mount Sinai Hospital, a series of nine papers[3] was published in August, 1940, which presents the most recent data on massive arsenotherapy in early syphilis (the five-day treatment of early syphilis).

Method of Treatment.—From 1933 to 1938, neoarsphenamin was used in treating ninety-three patients with primary or secondary syphilis by the five-day method. A freshly prepared solution, consisting of 0.1 gram neoarsphenamin dissolved in 100 cubic centimeters of 5 per cent glucose, was administered by intravenous drip at the rate of

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TABLE 1.—*Therapeutic Results Obtained With Neoarsphenamin*

Patients	Duration of Follow-up Study	Number of Patients Treated	Negative Serologic Reactions; Clinical Cures		Failures;* Clinical or Serologic Relapse	Maximum Per Cent of Failure
1933 group	6 years	15	13	86%	2	13.4
1937 group	2 years	78	71	91%	7	9.0
Total		93	84	90.3%	9	9.7

* Including doubtful seropositive results.

3 cubic centimeters per minute for ten hours a day during five successive days. Thus, the total dose of neoarsphenamin was 4 to 4.5 grams. Because of a death from hemorrhagic encephalitis following this treatment, mapharsen, being considered a less toxic drug, was substituted for neoarsphenamin in 1938. With the exception of one, all patients treated were males.

Two series of patients were treated with neoarsphenamin, one group in 1933 and the other in 1937. The former was followed for six and the latter for two years. Table 1 shows the therapeutic results obtained with neoarsphenamin.

All the patients who were lost, from observation, are included in the percentage of maximum failure, and those in whom there was any doubt as to the therapeutic results were classified as failures. Even with this rigid analysis, the percentage of clinical cures was high, *i. e.,* 90.3 per cent.

Toxic Effects from Neoarsphenamin.—Many toxic reactions were encountered in the patients treated with neoarsphenamin. The untoward effects from both neoarsphenamin and mapharsen as given by Chargin are listed in Table 2.

The incidence of primary and secondary fever, transient erythema, jaundice, and peripheral neuritis was rather high. In the primary, or Herxheimer fever, the temperature rose sharply, averaging 102 degrees Fahrenheit on the first day of treatment; it usually subsided to normal by the next morning. The highest temperature noted in primary fever was 105 degrees Fahrenheit, and the longest duration was four days. The secondary fever appeared toward the end of the treatment period; the temperature averaged 102.8 degrees Fahrenheit for four days, the highest temperature was 105.4 degrees Fahrenheit and the longest duration ten days. In some cases the secondary fever was accompanied by erythema. The toxicoderma was mild, of short duration and did not sensitize the patient to the drug. The high percentage of this reaction is noteworthy. The incidence of peripheral neuritis (35 per cent) in patients treated with neoarsphenamin was exceedingly high, and while in most cases the reaction was mild it lasted for four to six months in several instances.

It is obvious from Table 2 that the percentage of toxic reactions caused by mapharsen was much smaller than that brought about by neoarsphenamin. Mapharsen, therefore, may be considered a safe drug for this purpose.

Treatment with Mapharsen.—As previously stated, treatment with mapharsen was begun in the fall of 1938. At first, 10 per cent of the dose of neoarsphenamin, or 400 milligrams, was given. Because of the low toxicity, the dose was slowly increased to 1,200 milligrams. The patients treated were divided into two groups. *Group A* consisted of 157 patients, who received less than 1,200 milligrams of mapharsen and were followed for eighteen months. Of these, twenty-four received

TABLE 2.—*Untoward Effects from Neoarsphenamin and Mapharsen*

	Neoarsphenamin		Mapharsen	
	Number	Per Cent	Number	Per Cent
Total treatment courses 399 treatment cases	111		288	
Primary fever	69	62	116	40
Secondary fever	71	64	36	12
Toxicoderma	50	45	33	11
Dermatitis exfoliativa	1	0.9	0	0
Blood dyscrasias	0	0	0	0
Renal damage	0	0	0	0
Jaundice	4	3.6	2	0.7
Peripheral neuritis	39	35	5	1.6
Cerebral symptoms	2	1.8	3	1.04
Hemorrhagic encephalitis	(1)	(0.9)	(1)	(0.34)
Single convulsions	(1)	(0.9)	(1)	(0.34)
Disorientation	(0)	(0)	(1)	(0.34)
Fatality	1	0.9	0	0

less than 600 milligrams; thirty received approximately 700 milligrams; twenty-seven, 800 milligrams; forty-nine, 1,000 milligrams; and twenty-seven, 1,100 milligrams. *Group B* consisted of one hundred patients, who received 1,200 milligrams of mapharsen and were followed for only six months. An evaluation of the therapeutic results obtained in Group A showed satisfactory results in 72 per cent. This number included all those who were classified as failures. The period of observation in Group B has been too short to evaluate the therapeutic results. To the present time the therapeutic results from mapharsen appear inferior to those from neoarsphenamin, although the toxicity of the former is definitely less than that of the latter.

COMMENT

The proponents of massive arsenotherapy in early syphilis set forth its advantages as follows:

1. By this method the infectious lesions of early syphilis are rapidly sterilized. Treponema pallida disappear within twenty-four to forty-eight hours, and the lesions remain free of spirochetes and heal rapidly.
2. Only five days are required to complete the course of treatment. Thus, the prolonged treatment over a period of two or three years, necessitated by the present methods of multiple injections, is eliminated.
3. All patients who are placed under treatment complete their course. In contrast, 20 to 80 per cent of the patients treated by the usual methods disappear from observation before therapy is completed.
4. The percentage of satisfactory therapeutic results is as great, or greater, than in the methods now in use.
5. A massive sterilizing dose of a spirocheticide accomplishes the primary aim of Ehrlich.
6. Administration of massive doses of the arsphenamins by the continuous drip method eliminates the phenomenon of speed shock.
7. Serious toxic reactions may be avoided by substituting mapharsen for neoarsphenamin.

The disadvantages of the massive arsenotherapy in early syphilis may be stated as follows:

1. The five-day treatment is still in the experimental stage. It should, therefore, be thoroughly investigated in hospitals equipped to carry out the procedure and to do proper follow-up studies before it is submitted for general application by practicing physicians and by clinics. A period of several years will probably be required to accomplish this.
2. It is a hospital procedure and entails considerable expense.
3. Sufficient time has not elapsed to evaluate the final therapeutic results and the toxic end-effects.
4. Neoarsphenamin is too toxic to be practical for application by this method.
5. Mapharsen is definitely less toxic than neoarsphenamin and may be used in its place. However, it has been employed for too short a time to determine its therapeutic value. To date, the therapeutic results with mapharsen have not been as satisfactory as those reported with the use of neoarsphenamin.
6. This method has been employed only in males with early syphilis. Therefore, no data are available as to its value in the treatment of early syphilis in females, of latent syphilis, or of the numerous manifestations in late syphilis.

Two other points mentioned in these publications[3] warrant further discussion. The original investigators state that 4 to 4.5 grams of neoarsphenamin may be given by the massive dose method in five days, while three months are required for this dosage by the usual methods of antisyphilitic treatment. I wish to point out that by the usual methods of treatment of early syphilis we administer 4.35 grams of neoarsphenamin in six weeks; in some clinics an even higher dosage is used. I am certain that, if it seemed advisable, this dosage could safely be increased further by the use of the multiple injection method.

Secondly, I disagree with the statement that the incidence of hemorrhagic encephalitis in the cases reported,[3] namely, two in 350 with death in one, is not excessive. The authors quote Cole[4] as reporting that the incidence of deaths due to hemorrhagic encephalitis in syphilis treated by the usual methods is one in 200 cases. Moore pointed out that hemorrhagic encephalitis was noted at Johns Hopkins Hospital in only one of 15,000 cases under treatment. Stokes[5] stated that a mortality rate from all causes of one in 15,000 to 35,000 injections of the arsphenamins may be considered good technical performance. Under the most favorable conditions the unavoidable risk of antisyphilitic treatment is much less. Since hemorrhagic encephalitis is responsible for 50 per cent of all deaths due to the arsphenamins, fatalities as a result of this reaction are obviously rare. This finding coincides with the experience we have had at the University of California Clinic. During the past fifteen years we have encountered death from hemorrhagic encephalitis as a result of treatment with the arsphenamins in only one case.

CONCLUSIONS

Massive arsenotherapy of syphilis is at present entirely experimental. Many years of investigation are required before its true value in the treatment of syphilis can be determined. It has been tried only in the primary and secondary stages of syphilis in the male.

This method of antisyphilitic treatment should not be used by physicians or clinics in general. It should be employed only in institutions equipped to carry out the technique of the procedure and, what is more important, to follow the patients for a sufficient period of time to evaluate the therapeutic effects.

Much work must be done both clinically and on experimental animals before the most effective dose of the drug and the most advantageous period of treatment can be determined.

The five-day treatment of syphilis opens up a new avenue of approach to the control of early syphilis, and is an important contribution to the study of the problem of antisyphilitic therapy.

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RECURRENT LYMPHANGITIS*

REPORT OF A CASE WITH UNUSUAL FEATURES

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THE subject of lymphangitis is given scant treatment in textbooks on dermatology. In those on internal medicine and surgery it receives usually a few more lines, but in none at our disposal have we been able to find a detailed description of the topic under consideration. Recurrent lymphangitis, as the term is used here, is undoubtedly a clinical and biologic entity. Its cardinal characteristics are a diffuse, occasionally streaked erythema, involving any part of the body, but showing sites of predilection, and most commonly seen on the lower extremities. This erythema may cover a patch the size of a silver coin or completely involve two extremities or more; usually it is associated with some edema. Hence, it frequently has been referred to as chronic or recurrent erysipelas. During an attack the erythema frequently, although not always, is associated with palpable enlargement of the satellite glands. In very mild infections there may be no demonstrable rise of temperature, but usually there is a fever of 102 to 103 degrees Fahrenheit and we have seen an occasional rise to 106 degrees Fahrenheit. This syndrome might be simulated by other types of infection, but its most distinctive characteristic is its self-limited course, which varies from two to six days. Such an attack recurs every week or two or at intervals of several months, always shows the same characteristics, and in due time results in considerable thickening of the tissues and a veritable elephantiasis. Gans,[1] while he does not sharply depicture this syndrome, gives an accurate description of its histopathology in his chapter on early and late elephantiasis. This clinical syndrome is a reasonably common one, although probably not clearly recognized by the average practitioner; and, if personal experience can be relied upon, not even by all dermatologists. The case reported here, however, has shown some unusual features, observed by us in only this one patient out of a total of more than thirty.

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REPORT OF CASE

B. A., a man, aged thirty-three years, when first seen, in 1936, came with the history that the first symptoms were noticed ten years before; the erythema first was noticed on the inside of one foot. At that time a definite diagnosis of dermatophytosis of the feet was made elsewhere. While we could not demonstrate the mycotic organism during the time he was under our care, we believe we can readily agree with that diagnosis since it is a very common mode of development. The attacks since then occurred at intervals of about two weeks, and have involved both legs, causing considerable thickening. Six years after the beginning of the process on the legs there was involvement of both hands which also showed considerable enlargement, although less than the legs. For several years prior to consultation with us he had developed an eruption with vesiculation, oozing, crusting, scaling, fissuring—in brief, all the characteristics of a severe dermatitis. The case was unique in that this dermatitis, which involved almost the entire skin, coincided with the febrile attacks. As the patient noted his recurrence of local erythema and systemic symptoms, the dermatitis became severe and subsided as promptly as the other acute symptoms. During several years of observation he also showed marked sensitiveness to soap, turpentine, gasoline, paint, and various other substances. Trichophytin tests were repeatedly positive. An attempt to treat him with sulfanilamide showed marked sensitiveness to ten grains three times daily, and produced marked photosensitiveness for a period of time. He has now been free from acute exacerbations for about one and one-half years. A residual induration of the tissues of the hands and feet constitute some impediment, but he is able to do some regular work where formerly he was totally disabled.

COMMENT ON CASE

It is the first case we have observed in which an eczematoid eruption was definitely a part of the syndrome of recurrent lymphangitis. The eruption was always synchronous with the febrile attack, indicating an etiologic relationship. Previous studies of our own and those of other observers point to the streptococcus or possibly to a mixed infection in the lymphatics as the cause of recurrent lymphangitis. Therefore, this case adds marked evidence to the conception that a focus of pyogenic infection can play at least a part in the production of an eczema. We are not unmindful, however, of the complex interplay of such an infection with the trichophyton, external irritation, and possibly some associated systemic abnormality, which Wise[2] has so beautifully emphasized in regard to vesicular eruptions of the hands and feet. It is evident that the patient's skin had undergone an allergic change, as shown by his hypersensitiveness to banal external irritants, to sulfanilamide with its ready production of photosensitiveness, and his very active response to trichophytin. Whatever the exact mechanism, there is no doubt that activity of the infection focus in the lymphatics acted as the precipitating cause, as the match, as it were, that produced the explosion.

We hope this case will serve to call particular attention to the syndrome of recurrent lymphangitis, to the end that its early recognition, on which depends much of its successful treatment, may penetrate wider medical circles, especially the general field. Long duration does not make the prognosis hopeless, however, as this case illustrates.